Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo[3.3.1.]nonane with Selected Organic Compounds Containing Representative Functional Groups

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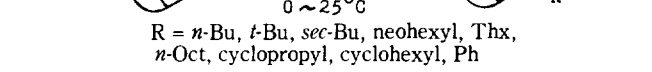
The approximate rates and stoichiometry of the reaction of excess potassium 9-*sec*-amyl-9-boratabicyclo[3.3.1.]nonane (K 9-*sec*-Am-9-BBNH) with selected organic compounds containing representative functional groups under standardized conditions (tetrahydrofuran, 0 °C) were examined in order to explore the reducing characteristics of the reagent for selective reductions. The reagent readily reduces aldehydes, ketones, acid chlorides and epoxides to the corresponding alcohols. However, carboxylic acids, aliphatic nitriles, *t*-amides, and some sulfur compounds show very little reactivity or no reactivity to this reagent. The most interesting feature of the reagent is that aromatic nitriles are reduced moderately to the corresponding aldehyde stage, whereas aliphatic nitriles are inert. In addition, the reagent shows a high stereoselectivity toward cyclic ketones at 0 °C and −25 °C. The selectivity exhibited at 0 °C is comparable to that by lithium trisiamylborohydride at that temperature.

Introduction

Trisubstituted borohydrides such as trialkyl- or trialkoxyborohydrides have appeared to be a highly attractive class of reducing agents in organic synthesis. Trialkylborohydrides have proven to be powerful selective reducing agents.[2] On the other hand, trialkoxyborohydrides were proved to be very mild reducing agents.[3] Recently a general procedure for the syntheses of mixed alkoxyalkylborohydrides such as dialkylmonoalkoxy-[4] and dialkoxymonoalkylborohydrides[5] has been established and they have been proved to be highly stereoselective reducing agents.[4]

Very recently, we reported a general synthesis of a new class of reducing agents, potassium 9-alkyl-9-boratabicyclo-[3.3.1]nonanes (K 9-R-9-BBNHs), containing a wide variety of alkyl groups by treating the corresponding 9-alkyl-9-BBNs with excess potassium hydride in THF (eq. 1)[6].



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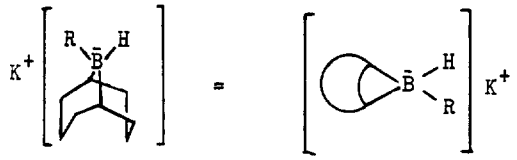
R = *n*-Bu, *t*-Bu, *sec*-Bu, neohexyl, Thx, *n*-Oct, cyclopropyl, cyclohexyl, Ph

In the course of a systematic study of stereoselectivity toward cyclic ketones of these reagents, we found that some of these reagents exhibited an excellent stereoselectivity.[6,7].

Therefore, we decided to explore the reducing characteristics of these reagents. We chose potassium 9-*sec*-amyl-9-BBNH as a representative for the series and undertook a systematic study on the approximate rates and stoichiometry for the reaction of excess K 9-*sec*-Am-9 BBNH with the standard list of selected organic compounds containing representative functional groups under standardized conditions (THF, 0 °C).



Results and Discussion

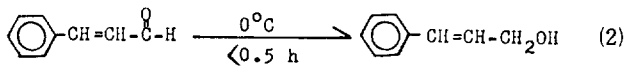
Preparation of the Reagent, and Procedure for Rates and Stoichiometry Studies.

K 9-*sec*-Am-9-BBNH was prepared by adding the neat 9-*sec*-Am-9-BBN to a vigorously stirred suspension of *ca.* 50 mole % excess potassium hydride (free of oil) in THF at 25 °C for 6 h. 9-*sec*-Am-9-BBN was prepared by hydroborating 2-methyl-2-butene with 9-BBN. The reagent was stable at 0 °C at least for 6 months. The procedure for the systematic study involved preparation of a reaction mixture of the reagent (1.0 M in hydride) and the compound examined (0.25 M) under study in THF at 0 °C. Hydrogen evolution during the reaction was measured by using a gas buret. A blank reaction was run under identical conditions, but without addtion of the compound. At the appropriate reaction intervals, aliquots were withdrawn from the reaction mixture and analyzed for residual hydride by hydrolysis.[8] From the difference in the volume of hydrogen evolution in the two case, the hydride used by the compound for reduction was calculated. In this way, it was possible to calculate a value for the number of moles of the hydride consumed by the compound to evolve hydrogen and the number of moles of hydride utilized for the reduction.[8]

Alcohols, Phenols, Amines, and Thiols (Active Hydrogen Compounds). Primary alcohol evolved hydrogen completely within 3 h, whereas secondary and tertiary alcohols evolved only a partial equiv of hydrogen. Benzyl alcohol, phenol, benzenethiol evolved 1 equiv of hydrogen immediately, while *n*-hyxylamine evolved only slightly.

The rate of hydrogen evolution for alcohols decreases in the order of aromatic>primary>secondary>tertiary. The results are summarized in Table 1.

Aldehydes and Ketones. The aldehydes and ketones examined rapidly utilized 1 equiv of hydride rapidly at 0 °C to proceed to the alcohol stage. Cinnamaldehyde, an α,β-unsaturated carbonyl compound, consumed 1 equiv of hydride immediately, and no further hydride uptake was apparent even after 24 h. This means that K 9-*sec*-Am-9-BBNH reduces the aldehyde group cleanly without affecting the double bond to produce cinnamyl alcohol (eq. 2).



(2)

The results are summarized in Table 2.

Table 1. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Active Hydrogen Compounds in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
1-hexanol	0.5	0.88	0.88	0.00
	1.0	0.94	0.94	0.00
	3.0	1.00	1.00	0.00
benzyl	0.5	1.00	1.00	0.00
alcohol	1.0	1.00	1.00	0.00
3-hexanol	0.5	0.08	0.08	0.00
	3.0	0.24	0.24	0.00
	24.0	0.57	0.57	0.00
	96.0	0.81	0.81	0.00
3-ethyl-3-	0.5	0.02	0.02	0.00
pentanol	6.0	0.05	0.05	0.00
	48.0	0.09	0.09	0.00
	144.0	0.20	0.20	0.00
phenol	0.5	1.02	1.02	0.00
	1.0	1.02	1.02	0.00
n-hexyl-	0.5	0.02	0.02	0.00
amine	6.0	0.03	0.03	0.00
	24.0	0.04	0.04	0.00
1-hexane-	0.5	0.53	0.53	0.00
thiol[c]	3.0	0.59	0.59	0.00
	24.0	0.75	0.75	0.00
benzene-	0.5	1.04	1.04	0.00
thiol[c]	1.0	1.04	1.04	0.00

[a] 9 Mmol of compound to 36 mmol of K 9-*sec*-Am-9-BBNH (36 mmol of hydride) in 36 m*l* of solution; 0.25 M in compound and 1.0 M in hydride. [b] Millimoles/millimole of compound. [c] Gelatinous white precipitate.

Table 2. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Aldehydes and Ketones in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
caproaldehyde	0.5	0.02	1.02	1.00
	1.0	0.02	1.02	1.00
benzaldehyde	0.5	0.01	1.03	1.02
	1.0	0.01	1.03	1.02
2-heptanone	0.5	0.00	1.03	1.03
	1.0	0.00	1.03	1.03
norcamphor	0.5	0.02	1.03	1.01
	1.0	0.02	1.03	1.01
acetophenone[c]	0.5	0.00	1.00	1.00
	1.0	0.00	1.00	1.00
benzophenone	0.5	0.01	1.01	1.00
	1.0	0.01	1.01	1.00
cinnamaldehyde	0.5	0.00	1.01	1.01
	24.0	0.00	1.02	1.02

[a,b] See the corresponding footnotes in Table 1. [c] Immediately turned to orange color.

Table 3. Stereochemistry of Cyclic Ketone Reduction with Potassium 9-*sec*-Amyl-9-boratabicyclo[3.3.1]nonane and Other Representative Reagents in Tetrahydrofuran[a,b,c]

ketone	temp (°C)	K 9-*sec*-Am-9-BBNH	9-BBN[d]	K 9-O-*t*-Am-9-BBNH[e]	Li *sec*-Bu_3BH[f]	$LiSia_3BH$[e]
cyclohexanone						
2-methyl-	0	99.5	40	97	99.3	99.4
	- 25	99.5	—	97.5	—	—
3-methyl-	0	96	12	84	85	98
	- 25	96.5	—	86.5	—	—
4-methyl-	0	90	—	77.5	80.5	93
	- 25	90.5	—	80.5	—	—
4-*tert*-	0	96.5	8	83	87.5	96.5
butyl-	- 25	96.5	—	88	—	—
3,3,5-tri-	0	99	—	>99.9	99.8	99
methyl-	- 25	99.5	—	>99.9	—	—
norcamphor	0	95.5	91	97	99.6	99
	- 25	96	—	98.5	—	—
camphor	0	99.9	75	93	99.6	99.9
	- 25	99.9	—	93.5	—	—

[a] A 2:1 ratio for reagent: ketone was utilized. [b] The yields of alcohols were quantitative. [c] The figures are percentage of the less stable isomers. [d] Data taken from ref. 9. [e] Data taken from ref. 4-a [f] Data taken from ref. 10.

Table 4. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Quinones in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
p-benzoquinone[c]	0.5	0.16	1.08	0.92
	1.0	0.20	1.13	0.93
	3.0	0.26	1.21	0.95
	6.0	0.32	1.27	0.96
	24.0	0.35	1.31	0.96
anthraquinone[d]	0.5	0.01	1.07	1.06
	1.0	0.01	1.21	1.20
	3.0	0.02	1.31	1.29
	6.0	0.02	1.43	1.41
	24.0	0.02	1.73	1.71

[a,b] See the corresponding footnotes in Table 1. [c] The immediately-formed dark green color turned to dark brown precipitate. [d] Reverse addition (solution of reagent was added to suspension of compound).

The stereoselectivity of the reagent on the reduction of representative cyclic ketones was also studied, and the results and comparable data for the other reagents are summarized in Table 3. The introduction of *sec*-amyl group, a α-methyl substituted tertiary alkyl group, enhances the stereoselectivity tremendously, comparable to the results achieved at 0 °C with lithim trisiamylborohydride.

Quinones. *p*-Benzoquinone rapidly consumed 1.08 equiv of hydride, of which 0.16 equiv was utilized for hydrogen evolution and the remaining 0.92 for reduction. The hydride consumption for further reduction was almost ceased with the continuous slow evolution of hydride. Anthraquinone ap-

Table 5. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
caproic	0.5	1.01	1.01	0.00
acid	24.0	1.01	1.03	0.02
	120.0	1.01	1.05	0.04
benzoic	0.5	0.97	0.97	0.00
acid	1.0	1.01	1.01	0.00
	48.0	1.01	1.04	0.03
acetic	0.5	0.02	1.39	1.37
anhydride	3.0	0.02	1.83	1.81
	24.0	0.02	2.17	2.15
	144.0	0.02	2.17	2.15
succinic	0.5	0.01	1.36	1.35
anhydride	3.0	0.01	1.68	1.67
	6.0	0.01	2.02	2.01
	24.0	0.01	2.77	2.76
phthalic	0.5	0.01	1.30	1.29
anhydride	3.0	0.01	1.38	1.37
	24.0	0.01	1.60	1.59
	120.0	0.01	1.68	1.67
caproyl	0.5	0.05	2.08	2.03
chloride	1.0	0.05	2.08	2.03
benzoyl	0.5	0.00	1.50	1.50
chloride	3.0	0.00	1.84	1.84
	6.0	0.00	2.00	2.00

[a,b] See the corresponding footnotes in Table 1.

Table 6. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Esters and Lactones in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
ethyl	0.5	0.00	0.17	0.17
caproate	3.0	0.00	0.38	0.38
	6.0	0.00	0.62	0.62
	24.0	0.00	0.96	0.96
	48.0	0.00	1.47	1.47
	144.0	0.00	1.98	1.98
ethyl	0.5	0.00	0.19	0.19
benzoate	1.0	0.00	0.30	0.30
	3.0	0.00	0.62	0.62
	6.0	0.00	0.95	0.95
	24.0	0.00	1.32	1.32
	48.0	0.00	1.99	1.99
phenyl	0.5	0.00	1.98	1.98
acetate[c]	1.0	0.00	1.99	1.99
r-butyro-	0.5	0.00	1.97	1.97
lactone	1.0	0.00	2.01	2.01
phthalide[d]	0.5	0.00	2.00	2.00
	1.0	0.00	2.00	2.00
isopropenyl	0.5	0.00	1.99	1.99
acetate	24.0	0.00	2.00	2.00

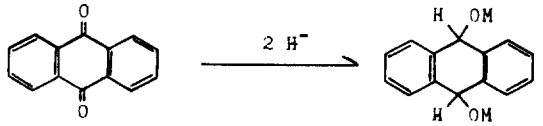
[a] See the corresponding footnotes in Table 1. [c] Gelatinous white precipitate. [d] Yellow color.

Table 7. Reaction of Potassium 9-*sec*-Amyl-9-boratobicyclo-[3.3.1]nonane with Representative Epoxides in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
1,2-butylene	0.5	0.00	1.00	1.00
oxide	1.0	0.00	1.00	1.00
styrene	0.5	0.00	1.01	1.01
oxide	1.0	0.00	1.01	1.01
cyclohexene	0.5	0.00	0.58	0.58
oxide	1.0	0.00	0.66	0.66
	3.0	0.00	0.82	0.82
	6.0	0.00	1.00	1.00

[a,b] See the corresponding footnotes in Table 1.

proached to the utilization of 2 equiv hydride for reduction with essentially no hydrogen evolved, suggesting the formation of 9,10-dihydroxy intermediate (eq. 3).



(3)

The results are summarized in Table 4.

Carboxylic Acids and Acyl Derivatives. Both caproic and benzoic acids evolved hydrogen rapidly and quantitatively. However, no reduction was observed. On the other hand, acid chlorides were reduced to the corresponding alcohols readily. Acid anhydrides consumed first equiv of hydride at a fast rate, but the subsequent reduction proceeded relatively slowly. The results are summarized in Table 5.

Esters and Lactones. Ethyl caproate and ethyl benzoate reacted with this reagent slowly. In order to examine the possibility for obtaining the aldehydes from esters, the limiting amount of the reagent was applied for the partial reduction. However, the yield for such transformation appeared not to be satisfactory. Thus, ethyl caproate and ethyl benzoate were converted to the corresponding aldehydes in yields of 50 and 37%, respectively, both in 24 h at 0°C. On the other hand, phenyl acetate and isopropenyl acetate rapidly used 2 equiv of hydride, undergoing reduction to the alcohol stage. Also lactones rapidly utilized 2 equiv of hydride to the diol stage. The results are summarized in Table 6.

Epoxides. The reagent reacted with 1,2-butylene oxide and styrene oxide rapidly, but reacted with cyclohexene oxide at a moderate rate to the corresponding alcohol stages. The results are summarized in Table 7.

Amides and Nitriles. Both primary amides examined, such as caproamide and benzamide, evolved hydrogen partially, and the subsequent reduction was sluggish or inert. Tertiary amides examined also reacted with the reagent only very slowly. In the reduction of nitriles, we can find a very interesting feature. The typical aliphatic nitrile, caprylonitrile, appeared to be essentially inert to this reagent, not showing any detectable sign to be reduced even in 5 days. However, the representative aromatic nitrile, benzonitrile, used the first hydride at a moderate rate and the subsequent second hydride relatively very slowly. This strongly indicates that the reagent can reduce aromatic nitriles to the corresponding aldehydes. In fact, a 92% yield of benzaldehyde was realized

Table 8. Reaction of Potassium 9-*sec*-Amyl-9-borataticyclo-[3.3.1]nonane with Representative Amides and Nitriles in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for redction[b]
caproamide	0.5	0.27	0.28	0.01
	1.0	0.37	0.38	0.01
	6.0	0.64	0.65	0.01
	24.0	0.82	0.84	0.02
	72.0	0.90	0.92	0.02
benzamide	0.5	0.74	0.79	0.05
	3.0	0.76	0.98	0.22
	24.0	0.77	0.99	0.22
N,N-dimethyl-	0.5	0.00	0.05	0.05
caproamide	1.0	0.00	0.08	0.08
	3.0	0.00	0.12	0.12
	6.0	0.00	0.19	0.19
	24.0	0.00	0.23	0.23
	48.0	0.00	0.35	0.35
N,N-dimethyl-	1.0	0.00	0.00	0.00
benzamide	6.0	0.00	0.01	0.01
	48.0	0.00	0.05	0.05
capryloni-	0.5	0.00	0.00	0.00
trile	120.0	0.00	0.02	0.02
benzonitrile	0.5	0.00	0.09	0.09
	1.0	0.00	0.15	0.15
	6.0	0.00	0.36	0.36
	24.0	0.00	0.75	0.75
	48.0[c]	0.00	1.01	1.01
	72.0	0.00	1.08	1.08
	120.0	0.00	1.35	1.35

[a,b] See the corresponding footnotes in Table 1. [c] Reaction mixture was analyzed with (2,4-dinitrophenyl) hydrazine, showing the 92% yield of benzaldehyde.

by analyzing the reaction mixture in 48 h with (2,4-dinitrophenyl) hydrazine. Accordingly, this reagent could offer the possibility for the partial reduction of only the aromatic nitriles to aldehydes selectively in the presence of aliphatic nitirles intact. This possibility is under investigation extensively and will be published shortly[11]. The results are summarized in Table 8.

Nitro compounds and Their Derivatives. 1-Nitropropane rapidly evolved 1 equiv of hydrogen, forming a white precipitate with no hydride consumption for reduction. Presumably, the active α-hydrogen seems to be involved in this reaction (eq. 4).

$$CH_3CH_2CH_2NO_2 + K\ 9\text{-}sec\text{-}Am\text{-}9\text{-}BBNH \longrightarrow CH_3CH_2CH{=}N^{+}\langle^{O^-}_{OK} \downarrow + H_2 \uparrow \quad (4)$$

Nitrobenzene utilized 1 equiv of hydride for reduction rapidly and the subsequent hydride uptake was very slow with the slight hydrogen evolution. Azobenzene underwent reduction slowly, with no hydrogen evolution. The results are summarized in Table 9.

Other Nitrogen Compounds. Cyclohexanone oxime

Table 9. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
1-nitro-	0.5	0.98	0.98	0.00
propane	1.0	1.00	1.00	0.00
nitro-	0.5	0.02	1.12	1.10
benzene[d]	3.0	0.07	1.27	1.20
	6.0	0.10	1.35	1.25
	24.0	0.14	1.44	1.30
	48.0	0.16	1.53	1.37
azobenzene[e]	0.5	0.00	0.12	0.12
	1.0	0.00	0.20	0.20
	6.0	0.00	0.30	0.30
	24.0	0.00	0.43	0.43
	72.0	0.00	0.51	0.51

[a,b] See the corresponding footnotes in Table 1. [c] White precipitate. [d] Orange color precipitate. [e] Dark brown precipitate.

Table 10. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Other Nitrogen Compounds in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
cyclohexanone	0.5	1.01	1.03	0.02
oxime	24.0	1.01	1.03	0.02
phenyl	0.5	0.00	1.00	1.00
isocyanate	24.0	0.00	1.00	1.00
pyridine	0.5	0.00	0.69	0.69
	1.0	0.00	0.80	0.80
	3.0	0.00	1.01	1.01
	6.0	0.00	1.02	1.02
	24.0	0.00	1.24	1.24
	48.0	0.00	1.27	1.27
pyridine	0.5	0.00	0.70	0.70
N-oxide[c]	1.0	0.00	1.02	1.02
	3.0	0.00	1.32	1.32
	6.0	0.00	1.42	1.42
	24.0	0.00	1.85	1.85
	48.0	0.00	1.91	1.91

[a,b] See the corresponding footnotes in Table 1. [c] Red color.

rapidly evolved 1 equiv of hydrogen, without undergoing reduction. Phenyl isocyanate was rapidly reduced, utilizing 1 equiv of hydride, corresponding to reduction to the formanilide stage. Pyridine and pyridine N-oxide underwent a moderate reduction without hydrogen evolution, apparently the pyridine ring being attacked. The results are summarized in Table 10.

Sulfur Compounds. Both aliphatic and aromatic disulfides were reduced to the thiol stage rapidly, consuming 2 equiv of hydride, one for the evolution of hydrogen and the other for reduction. Dimethyl sulfoxide was absolutely inert to this reagent, whereas diphenyl sulfone was reduced slowly. Sulfonic acid, such as methanesulfonic acid and *p*-toluene-

Table 11. Reaction of Potassium 9-*sec*-Amyl-9-boratabicyclo-[3.3.1]nonane with Representative Sulfur Derivatives in Tetrahydrofuran at 0°C

compounds[a]	time (hr)	hydrogen evolved[b]	hydride used[b]	hydride used for reduction[b]
di-n-butyl	0.5	1.00	1.58	0.58
disulfide[c]	1.0	1.00	1.76	0.76
	3.0	1.00	2.01	1.01
diphenyl	0.5	1.01	1.13	0.12
disulfide[c]	1.0	1.01	1.69	0.68
	3.0	1.01	1.96	0.95
	6.0	1.01	2.03	1.02
dimethyl	0.5	0.00	0.00	0.00
sulfoxide	24.0	0.00	0.00	0.00
diphenyl	0.5	0.00	0.04	0.04
sulfone[c]	6.0	0.00	0.15	0.15
	24.0	0.00	0.23	0.23
	72.0	0.00	0.51	0.51
methanesul-	0.5	1.02	1.02	0.00
fonic acid	1.0	1.02	1.02	0.00
p-toluene-	0.5	3.05	3.05	0.00
sulfonic acid	1.0	3.05	3.05	0.00
monohydrate	3.0	3.05	3.05	0.00

[a,b] See the corresponding footnotes in Table 1. [c] White precipitate.

sulfonic acid, evolved hydrogen immediately and quantitatively, but no sign for reduction was observed. The results are summarized in Table 11.

Conclusion

K 9-*sec*-Am-9-BBNH has appeared to be a mild selective reducing agent in this systematic study. The reagent can reduce readily aldehydes, ketones, acid chlorides, and epoxides to the corresponding alcohol stages. Aromatic nitriles are reduced moderately to aldehyde stage, whereas aliphatic nitriles are essentially inert to this reagent. This strongly indicates the possibility for the partial reduction of only the aromatic nitriles to aldehydes in the presence of aliphatic nitriles intact. In addition, the reagent shows very little reactivity or no reactivity toward *t*-amide and some sulfur compounds. Furthermore, the reagent shows high stereoselectivity toward cyclic ketones, comparable to that by lithium trisiamylborohydride achieved at 0 °C. This unique reducing characteristics should find very useful applications in organic synthesis.

Experimental Section

All glassware used was predried at 140 °C for several hours, assembled hot, and cooled under a stream of nitrogen. All reactions were carried out under a static pressure of nitrogen in flasks fitted with a septum-covered side arm with use of standard techniques for handling air-sensitive materials.[8] Tetrahydrofuran (THF) was dried over a 4 Å molecular sieve and distilled for sodium-benzophenone ketyl prior to use. Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation or recrystallization when necessary. Some compounds were synthesized by using standard procedures. In all of the cases, physical constants agreed satisfactorily with constants in the literature. ^{11}B NMR spectra were recorded on a Bruker WP 80 SY Spectrometer, and all ^{11}B NMR chemical shifts are reported relative to $BF_3 \cdot OEt_2$.

Preparation of 9-*sec*-Am-9-BBN. An oven-dried, 500 m*l* roundbottomed flask with a side arm, equipped with a condenser leading to a mercury bubbler was flushed with dry nitrogen and maintained under a static pressure of nitrogen. To this flask were added 36.3 g (0.3 mol) of 9-BBN and 40 m*l* of THF, 21.3 g (0.3 mol) of 2-methyl-2-butene was added using syringe slowly with vigorous stirring. The reaction mixture was stirred for 6 h at room temperature. After then THF was removed by simple distillation and finally 48.7 g (yield; 85%) of 9-*sec*-Am-9-BBN was collected by distillation under the reduced pressure: bp 118 °C/12 mmHg, n_D^{20} 1.4809, ^{11}B NMR; δ = 87.9 ppm.

Preparation of K 9-*sec*-Am-9-BBNH in THF. Into an oven-dried 500 m*l* flask, equipped with a side arm, a condenser, and an adaptor connected to a mercury bubbler, was placed 43.6 g (0.38 mol) of potassium hydride as 35% oil suspension and the oil medium was removed by washing with THF (3 × 20 m*l*). To this oil-free potassium hydride were added 30 m*l* of THF and 47.8 g (0.25 mol) of 9-*sec*-Am-9-BBN prepared just before. The reaction mixture was stirred vigorously at 25 °C for 6 h to give k 9-*sec*-Am-9-BBNH, and the flask was kept in a refrigerator to settle down the excess potassium hydride. The resulting clear solution was standardized by removing an aliquot, hydrolyzing it with a 2N H_2SO_4-THF(1:1) mixture, and measuring the hydrogen evolved. With a series of preparations, the concentrations were determined to be about 1.5 M in K 9-*sec*-Am-9-BBNH. The THF solution of the reagent was characterized by a strong characteristic absorption in the IR at around 2000 cm^{-1} (ν, B-H) and by a clean doublet centered at −13.5 ppm (J_{B-H} = 67 Hz) in ^{11}B NMR.

General Procedure for Determination of Rates and Stoichiometry. To a 100 m*l* flask fitted with a side arm and a condenser leading to a gas buret was added 24 m*l* (36 mmol) of a 1.50 M THF solution of K 9-*sec*-Am-9-BBNH. The flask was immersed in an ice bath and the reaction mixture was diluted with 12 m*l* of THF containing 9 mmol of the compound to be examined. This makes the mixture 1 M in hydride and 0.25 M in the compound under investigation. At appropriate time intervals, 4 m*l* of aliquots were withdrawn and quenched in a time intervals, 4 m*l* of aliquots wer withdrawn and quenched in a 2N H_2SO_4-THF (1:1) hydrolyzing mixture. The hydrogen evolved was measured volumetrically. For the reaction of compounds with active hydrogen, the hydrogen evolved was collected in a gas buret and measured the volume of hydrogen. The reaction of benzoyl chloride is described as a representative procedure. After a 0.5 h reaction time at 0 °C, hydrolysis of a 4 m*l* aliquot of the reaction mixture indicated 2.50 mmol of residual hydride, which means that 1.50 mmol of hydride per mmol of benzoyl chloride had been consumed. After 6 h, the analysis showed 2.00 mmol of residual hydride, which indicated that the compound had been reduced to the corresponding alcohol. The results are summarized in Table 5.

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11. Preliminary experiments revealed that in the competitive reaction between benzonitrile and caprylonitrile with a limiting amount of the reagent a yield of 85% of benzaldehyde was formed and a 99% yield of caprylonitrile was recovered.

Synthesis and Reactions of Benzimidazoline-2-thione Derivatives

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Two properties of sodium naphthalenide (2), i.e. a strong base and a good electron donor were utilized for one pot synthesis: 2-alkylthiobenzimidazoles were synthesized in excellent yields from the reactions of benzimidazoline-2-thione (1) with an equimolar amount of alkyl halides in the presence of 2. Continueous addition of a different alkyl haldie without the isolation of 2-alkylthiobenzimidazoles afforded 1-alkyl-2-alkylthiobenzimidazoles having different alkyl goups at N and S atoms in excellent yields. Further addition of 2 to 1-alkyl-2-alkylthiobenzimidazoles gave excellent yields of 1-alkylbenzimidazoline-2-thiones. When 2 in THF was added to a suspension of 1-alkyl-2-alkylthiobenzimidazoles in THF, a bond cleavage between N and C of alkyl group as well as S and C of alkyl group occurred. This is in contrast to the observation in which only cleavage between S and C of alkyl group takes place in the homogeneous solution.

Introduction

It has been well known that a number of benzimidazoline-2-thione derivatives have significant biological activity such as fungicidal, virucidal, and antitumor activity.[1] This stimulated us to study the development of new synthetic methods of benzimidazoline-2-thione derivatives.

Synthesis of 1-alkyl-2-alkylthiobenzimidazoles has been achieved by the several methods. The most widely used method consists of the reactions of 2-alkylthiobenzimidazoles with excessive amounts of alkyl halides. Thus formed 1-alkyl-2-alkylthiobenzimidazolium halides were treated under basic conditions to give 1-alkyl-2-alkylthiobenzimidazoles in 80% yields.[2] Similarly reactions of benzimidazoline-2-thione (**1**) with alkyl halides in saturated sodium bicarbonate solution of isopropanol afforded 1,2-dialkylated compounds of **1** as minor products.[3]

Apart from these methods, there have been some reports for the synthesis of 1,2-dialkylated compounds of **1** which appear to be of limited usefulness.[4]

The characteristic of these methods lies in the two step processes, i.e., the formation of 2-alkylthiobenzimidazoles, followed by a alkylations at N-1 in aqueous alcohol to give low yields or the formation of 1-alkyl-2-alkylthiobenzimidazolium halides, followed by the removal of halogen acid using a base such as pyridine or potassium hydroxide.

We have developed one pot syntheses of 1-alkyl-2-alkylthio-benzimidazoles with two different alkyl groups and 1-alkylbenzimidazoline-2-thiones in dried THF using sodium naphthalenide (**2**) possessing two fundamental properties, i.e. a strong base and a good electron donor.

Results and Discussion

It has been shown that dialkylations at both N and S atoms of **1** can be readily achieved in almost quantitative